REMARKS

Claims 1-26 are pending in the present application.

Applicants have amended Claims 11, 12, 16-17, and 24-26 to replace the phrase ""a greater than additive effect" with the phrase "a synergistic effect in reducing blood glucose levels." Applicants have also amended Claims 11 and 12 to delete the phrase "or stabilizing the level of serum glucose."

Applicants maintain that the amendments add no new matter and are fully supported by the specification as originally filed. Support for the "synergistic effect" amendments to Claims 11, 12 and 24-26 can be found, for example, at Col. 2, lines 48-53 and Col. 2, lines 63-65. Support for the amendments to Claims 11 and 12 can be found, for example, at Col. 3, lines 5-6, as more fully discussed below.

Claims 1-26 are presented for examination. Applicants respond below to the specific rejections raised by the Examiner in the Office Action mailed November 11, 2004. For the reasons set forth below, Applicants respectfully traverse.

Objection under 37 C.F.R. §1.173(b)(2)

The Examiner has maintained the objection to an unspecified Amendment for alleged failure to comply with 37 C.F.R. §1.173(b)(2). Applicants understand that the Examiner is requesting that Applicants resubmit the claims in underlined form. Applicants submit herewith a listing of the claims, which indicates the current amendments as well as the amendments set forth in Applicants' January 30, 2001 initial filing. Applicants have underlined Claims 11-26 that were newly added in Applicant's July 24, 2001 submission. Applicants request that the Examiner withdraw the objection under 37 C.F.R. §1.173(b)(2) accordingly.

Rejection under 35 U.S.C. §112, first paragraph – Written Description

The Examiner has rejected Claims 1-26 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the invention. The Examiner alleges that there is no written description support for the word "or" in the phrase "A method of reducing hyperglycemia or stabilizing the

level of serum glucose," in Claims 11-23. The Examiner also argues that there is no written support for the limitation "greater than additive effect," as recited in Claims 1-26.

The Legal Standard for Written Description

The test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is whether the disclosure "reasonably conveys to artisan that the inventor had possession at that time of the later claimed subject matter." *In re Kaslow*, 707 F.2d 1366, 1375, 2121 USPQ 1089, 1096 (Fed. Cir. 1983); see also *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The adequacy of written description support is a factual issue to be determined on a case-by-case basis. See e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield Co.*, 208 F.3d 989, 996 (Fed. Cir. 2000).

The Specification Provides Support for the Amendments to Claims 11 and 12

As noted above, whether the Applicant was in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including the level of knowledge and skill in the art, and the teaching provided by the specification.

Regarding the rejection of Claims 11-26, Applicant has amended Claims 11 and 12 to delete the phrase "or stabilizing the level of serum glucose," such that the Claims read "A method for reducing hyperglycemia comprising administering to an individual. . ." Applicant submits that the specification as filed provides sufficient support for the amendment. As discussed in the personal interview with the Examiner conducted on February 28, 2005, Applicant discloses the administration of chromium tripicolinate in combination with biotin "to reduce the requirement for insulin and/or diabetic drugs and to reduce several important risk factors associated with Type II diabetes." Specification, Col. 3, lines 3-6. The Abstract of the instant application discloses "[a] method for *treating Type II diabetes* by administering. . . a combination of chromic tripicolinate and biotin" (emphasis supplied). Applicant submits that it is well-recognized that the primary focus of therapy for Type II diabetes is the reduction of

hyperglycemia. As such, Applicant's teaching of the administration of chromium tripicolinate and biotin to reduce the requirement for insulin (which reduces hyperglycemia by increasing glucose uptake) makes clear that the Applicant contemplated use of the present method for reducing hyperglycemia.

Applicants submit herewith a first Declaration by James Komorowski, M.S., who has expertise in the field of metabolic disorders, including diabetes. In ¶4 of his first Declaration, Mr. Komorowski testifies that "hyperglycemia is a hallmark of Type II Diabetes." Mr. Komorowski also indicates that the primary goal of treatments for Type II Diabetes is to reduce hyperglycemia. Specifically, Mr. Komorowski testifies that "the most important factor in treating Type II Diabetes is the treatment of hyperglycemia." First Komorowski Decl., ¶4.

In support of his position, Mr. Komorowski cites to publications of the American Diabetes Foundation and the National Center for Disease Control. Mr. Komorowski references a "Position Statement" by the American Diabetes Foundation (ADA) entitled "Diagnosis and Classification of Diabetes Mellitus." (Exhibit 1 to First Komorowski Decl.). In the opening statement, the American Diabetes Foundation characterizes diabetes mellitus as metabolic disease "characterized by hyperglycemia." American Diabetes Association, (January 2005), *Diabetes Care*, Vol 28, Supplement 1, p. S37, Col. 1. The ADA recognizes several therapies for diabetes, including "oral glucose lowering agents" and insulin treatment to regulated blood glucose levels. The ultimate goal of the therapies discussed is reduction of hyperglycemia, as summarized by the ADA in its statement that "the degree of hyperglycemia [in diabetics] reflects the severity of the underlying metabolic process and its treatment more than the nature of the process itself." American Diabetes Association at p. S37, Col. 3.

The ADA's characterization of hyperglycemia as the core of diabetes, as well as the target for its treatment, is echoed in the National Center for Disease Control's (CDC) "Frequently Asked Questions: Basics About Diabetes." (Exhibit 2 to First Komorowski Decl., excerpted from: http://www.cdc.gov/diabetes/faq/basics.htm). The CDC defines diabetes as "a disease in which blood glucose levels are above normal." Exhibit 2, p. 1. The CDC states that people with diabetes must "keep blood glucose levels from going. . . too high." Exhibit 2, p. 2.

In view of the objective evidence presented above, Applicant submits that one skilled in the art, upon reading Applicant's disclosure, would readily appreciate that Applicant was in possession of the concept of administering chromic tripicolinate and biotin for reducing

hyperglycemia. As such, Applicant submits Claims 11 and 12 as amended meet the written description requirement and request that the Examiner withdraw the rejection under 35 U.S.C. § 112, first paragraph.

The Specification Provides Support for Amended Claims 1-26

Applicant turns to the Examiner's rejection of Claims 1-26 as allegedly lacking written description support for the phrase "greater than additive effect." With respect to the original claims, Applicant maintains that the specification as filed provides support for the phrase "greater than additive effect." A person of ordinary skill in the art would appreciate that the phrase in question means an effect greater than one would expect from simply combining two ingredients. This language has been found acceptable to the Patent Office in the past, both in issuing the original patent now under consideration, as well as issuing related Patent No. 5,789,401. Applicant understands and agrees with the philosophy that every potential minor ambiguity should be corrected during the original patent prosecution. However, in light of issued original claims in this case and issued claims in the related patent, the Applicant is understandably reluctant to take action here that might be misinterpreted as calling into question the support for those existing claims.

It is noted that the language in question appears in claims as originally filed, which form a part of the specification. It also appears in the abstract as filed. Thus, it is clear that the Applicant was in possession of the concept of a "greater than additive effect" at the time the application was filed. With respect to the meaning of the phrase, the Examiner's attention is further directed, for example, to Col. 2, lines 63-65, which states that the reduction "is markedly greater than what would be expected when either component is administered alone, thus indicating a synergistic effect." This is clearly what the language in question is describing.

With respect to Claims 11, 12, 16-17, and 24-26, in the interest of expediting prosecution, Applicant has replaced the phrase "greater than additive effect" with the phrase "a synergistic effect in reducing blood glucose levels." Note that in doing so, Applicant in no way suggests that the language in the original claims or the related patent is in any way defective or inadequate. To the contrary, as explained above, a person of ordinary skill would clearly understand the meaning of the phrase in question, which was disclosed verbatim in the original claims as filed

and in the abstract. Accordingly, Applicant requests that the Examiner withdraw the rejection under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph – Indefiniteness

The Examiner has rejected Claims 1-26 under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner asserts that the phrase "greater than additive effect" is unclear since it is not clear "what the effect is" and "it is not clear what the additive effect is greater than." Office Action at p. 3.

Applicant maintains that the phrase "greater than additive effect" is definite for the reasons discussed above. A person of ordinary skill, familiar with the specification and with Col. 2, lines 63-65, would understand the meaning of the phrase.

In view of the above amendments and arguments, Applicant requests that the Examiner withdraw the rejection of Claims 1-26 under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. §103(a) – Obviousness

The Examiner has variously rejected the pending claims as being unpatentably obvious over Wagstaff (US Patent No. 5,635,535), Anderson ((1997), *J. Amer. Coll. Nutr.*, Vol. 16(5): 404-410) and Maebashi et al. ((1993), *J. Clin. Biochem. Nutr.* Vol. 14: 211-218).

As discussed in the personal interview summarized above, Applicant submits herewith a Second Declaration of James Komorowski under 37 C.F.R. § 1.132 that establishes that the combination of chromic tripicolinate and biotin together produces unexpected results in lowering blood glucose levels, that surpass the level expected based on the administration of each agent alone. (Second Komorowski Decl.). Thus, Applicant submits that even assuming arguendo, that the Examiner established a *prima facie* case of obviousness over the cited references, the evidence submitted herewith suffices to rebut the same. There is simply no suggestion in the art that the two ingredients have a synergistic effect on glucose metabolism.

Mr. Komorowski presents evidence that the combination of chromium picolinate with biotin enhanced glucose uptake to unexpectedly high levels based on the stimulation of glucose uptake seen with chromium picolinate alone or biotin alone. Exhibit B to the Second Komorowski Decl. illustrates the change in insulin-mediated glucose uptake by skeletal muscle

cells for a variety of nutrients tested, with and without chromic tripicolinate. Mr. Komorowski states that the nutrients tested in this assay were chosen based on data that suggested beneficial effects on glucose metabolism. Second Komorowski Declaration, ¶6. Exhibit C to the Second Komorowski Decl. graphically illustrates that α-lipoic acid, arginine, selenium, and reservol had no unexpected effects, while biotin combined with chromic tripicolinate resulted in glucose uptake levels that exceeded the uptake levels of the individual ingredients.

Applicant submits that the arguments and evidence presented establishes that Claims 1-26 are not obvious over the cited art. Specifically, the references do not disclose the unexpected finding that chromium picolinate and biotin act synergistically to reduce blood glucose levels. In sum, Applicant has provided objective evidence in the form of the specification, experimental data, and a declaration under 37 C.F.R. § 1.132, showing that the combination of chromium picolinate and biotin results in unexpectedly pronounced effects regarding glucose uptake. In view of the above, Applicant requests that the Examiner withdraw the rejection under 35 U.S.C. § 103(a).

The Double Patenting Rejection

A terminal disclaimer over U.S. Patent No. 5,789,401 is submitted herewith, thereby overcoming the rejection.

CONCLUSION

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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